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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/652,242	09/02/2003	Shohei Tanaka	Q77228	1866

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EXAMINER	
HUI, SAN MING R	

ART UNIT	PAPER NUMBER
1617	

DATE MAILED: 12/15/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/652,242	TANAKA ET AL.	
	Examiner	Art Unit	
	San-ming Hui	1617	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *02 September 2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *9-12* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *9-12* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☒ Certified copies of the priority documents have been received in Application No. 09/869,122.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *9-2-03*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Applicant's preliminary amendments filed September 2, 2003 have been entered. The cancellation of claims 1-8 and the addition of claims 9-12 are acknowledged.

Claims 9-12 are pending.

Double Patenting

A rejection based on double patenting of the "same invention" type finds its support in the language of 35 U.S.C. 101 which states that "whoever invents or discovers any new and useful process ... may obtain a patent therefor ..." (Emphasis added). Thus, the term "same invention," in this context, means an invention drawn to identical subject matter. See *Miller v. Eagle Mfg. Co.*, 151 U.S. 186 (1894); *In re Ockert*, 245 F.2d 467, 114 USPQ 330 (CCPA 1957); and *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970).

A statutory type (35 U.S.C. 101) double patenting rejection can be overcome by canceling or amending the conflicting claims so they are no longer coextensive in scope. The filing of a terminal disclaimer cannot overcome a double patenting rejection based upon 35 U.S.C. 101.

Claims 9 and 11 are rejected under 35 U.S.C. 101 as claiming the same invention as that of claims 1-2 of prior U.S. Patent No. 6,727,233. This is a double patenting rejection.

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 10 and 12 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-3 of U.S. Patent No. 6,727,233 ('233). Although the conflicting claims are not identical, they are not patentably distinct from each other because '233 teaches the method of treating bone lesions caused by multiple myeloma through inhibiting the proliferation of myeloma cells and suppressing bone resorption employing 1-hydroxy-2-(imidazo[1,2a]pyridin-3-yl)ethane-1,1-bisphosphonic acid.

Although '233 does not expressly teach the herein claimed dosage of 1-hydroxy-2-(imidazo[1,2a]pyridin-3-yl)ethane-1,1-bisphosphonic acid, It would have been obvious to one of ordinary skill in the art at the time the invention was made to optimize the effective parameters such as dosage of the actives, absent evidence to the contrary.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claim 9 is rejected under 35 U.S.C. 103(a) as being unpatentable over Isomura et al. (US Patent 4,990,503 from the Information Disclosure Statement received September 2, 2003) in view of Aparicio et al. (Leukemia, 1998;12:220-229 from parent application 09/869,122) and Shipman et al. (British Journal of Haematology, 1997;98:665-672 from the IDS received September 2, 2003).

Isomura et al. teaches the heterocyclic bisphosphonic acid compounds, useful as bone resorption inhibitors, including 1-hydroxy-2-(imidazo[1,2a]pyridin-3-yl)ethane-1,1-bisphosphonic acid can be blended with other pharmaceutically acceptable carrier to form medical composition suitable for oral administration (See particularly Col. 7, line 7-19; col. 9, example 5). Isomura et al. also teaches that 1-hydroxy-2-(imidazo[1,2a]pyridin-3-yl)ethane-1,1-bisphosphonic acid possess a strong bone resorption inhibition activities which can be used in diseases such as metastatic osteocarcinoma (See col. 6, line 4-66, particularly Table 1). Isomura et al. also teaches the oral dosage of 1-hydroxy-2-(imidazo[1,2a]pyridin-3-yl)ethane-1,1-bisphosphonic acid to be useful in inhibiting bone resorption to be 0.1 to 10mg daily (See col. 7, line 7-19).

Isomura et al. does not expressly teach 1-hydroxy-2-(imidazo[1,2a]pyridin-3-yl)ethane-1,1-bisphosphonic acid is useful in a method of inhibiting proliferation of myeloma cells. Isomura et al. does not expressly teach the effective dosage of 1-

hydroxy-2-(imidazo[1,2a]pyridin-3-yl)ethane-1,1-bisphosphonic acid to be 1 to 20 mg or 3 to 10 mg.

Aparicio et al. teaches two structurally different bisphosphonates: Aredia (pamidronate) and zoledronate, are effective in suppressing bone resorption and in inducing apoptosis in multiple myeloma cells by inducing apoptotic fragmentation (See the abstract; also page 223, col. 2, second paragraph). Aparicio et al. also teaches that both pamidronate and zoledronate are effective in inhibiting proliferation of multiple myeloma cells (See particularly page 226, col. 1, third paragraph).

Shipman et al. teaches three structurally different bisphosphonates: clodronate, pamidronate and YM 175, are effective in reducing the cell number of human myeloma cells (See page 667, Figure 1). Shipman et al. also teaches pamidronate and YM 175 as effective in inducing DNA fragmentation in myeloma cells (See page 668, col. 2, second paragraph).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to employ 1-hydroxy-2-(imidazo[1,2a]pyridin-3-yl)ethane-1,1-bisphosphonic acid, in the herein claimed dosage, in a method of inhibiting proliferation of myeloma cells and/or suppressing bone resorption herein.

One of ordinary skill in the art would have been motivated to employ 1-hydroxy-2-(imidazo[1,2a]pyridin-3-yl)ethane-1,1-bisphosphonic acid, in the herein claimed dosage, in a method of both inhibiting proliferation of myeloma cells and/or suppressing bone resorption herein because various structurally distinct bisphosphonate compounds, pamidronate, zoledronate, clodronate, and YM 175, are known to be effective in

inducing apoptosis in myeloma cells by inducing apoptotic fragmentation in myeloma cells. Possessing the teaching of the cited prior art, one of ordinary skill in the art would be reasonably expected to employ any known bisphosphonate compound, including 1-hydroxy-2-(imidazo[1,2a]pyridin-3-yl)ethane-1,1-bisphosphonic acid, in the herein claimed method to inhibit the proliferation of myeloma cells and/or suppressing bone resorption. Furthermore, the optimization of result effect parameters (e.g., dosage range) is obvious as being within the skill of the artisan.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to San-ming Hui whose telephone number is (571) 272-0626. The examiner can normally be reached on Mon 9:00 to 1:00, Tu - Fri from 9:00 to 6:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreeni Padmanabhan, PhD., can be reached on (571) 272-0629. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

SAN-MING HUI
PATENT EXAMINER

San-ming Hui
Primary Examiner
Art Unit 1617